REMARKS

Claims 11, 14, 19 and 21 have been amended. Claims 13 and 20 have been cancelled. No new matter has been added. In view of the amendments above, claims 11-12, 14-15, 17-19, 21-23, 25 and 26 are now pending.

Rejection under 35 USC § 102

Claims 11-15, 17-19, 21-23, 25 and 26 were rejected under 35 USC § 102(b) as anticipated by Hevey et al. (U.S. Patent No. 4,228,237). Applicants note that claim 13 seems to have been inadvertently included in the rejection under 35 USC § 102(b). The rejection of claims 13 and 20 under 35 USC § 103 as set forth in the Final Office Action clearly states that Hevey et al. does not teach or suggest each and every element of claim 13 (see page 4, section 6 of Paper No. 15). This statement would preclude an anticipation rejection of claims 13 and 20. Accordingly, these remarks are submitted with the understanding that the rejection under 35 USC § 102(b) is currently asserted against claims 11-12, 14-15, 17-19, 21-23, 25 and 26, as they were presented in the Amendment and Request for Reconsideration filed on April 7, 2003 (Paper No. 14).

The rejection of claims 11-12, 14-15, 17-19, 21-23, 25 and 26 as anticipated by Hevey et al. has been obviated by appropriate amendment. Claim 13 has been incorporated into independent claim 11, and claim 20 has been incorporated into independent claim 19. As amended, independent claims 11

and 19 each recite a 2nd hapten or hapten-like molecule that is identical to or an analogue of a 1st hapten or hapten-like molecule. As noted by the Examiner at page 4, section 6 of the Final Office Action, Hevey et al. does not disclose a 2nd hapten or hapten-like molecule that is identical to or an analogue of a 1st hapten or hapten-like molecule. Accordingly, independent claim 11 and dependent claims 12, 14-15 and 17-18 which depend from claim 11, and independent claim 19 and dependent claims 21-23, 25 and 26 which depend from claim 19, are not anticipated by Hevey et al., as the reference does not disclose each and every element of the claims.

Rejection under 35 USC § 103

Claims 13 and 20 were rejected under 35 USC § 103(a) as being obvious over Hevey et al. in view of Huber et al. (U.S. Patent No. 5,219,764). Since claims 13 and 20 have been incorporated into independent claims 11 and 19 respectively, Applicants will demonstrate that the invention now defined by claims 11 and 19 would not have been made obvious by the references.

The Final Office Action asserts that Hevey et al. discloses several embodiments of an assay and methods that determine the presence and amount of a ligand using a biotin/avidin system. The Examiner asserts that at least one of these embodiments of Hevey et al. discloses all the recitations of the claims except for the recitations of a 2nd hapten or hapten-like molecule that is identical

to or an analogue of a 1st hapten or hapten-like molecule. The Examiner further asserts that it would have been obvious to use such 1st and 2nd haptens or hapten-like molecules in view of the disclosure of Huber et al. regarding homogenous assays and hapten-biotin conjugates.

The rejection of the claims under 35 USC § 103(a) is respectfully traversed. Applicants point out that the Examiner has not established a *prima facie* case of obviousness under 35 U.S.C. § 103 as a basis for rejection of these claims. In MPEP § 2143, the three basic elements of a valid *prima facie* case of obviousness in view of a reference are presented as:

1) Some suggestion or motivation to modify the reference or to combine reference teachings;
2) A reasonable expectation of success in the modification or combination; and
3) A teaching or suggestion of all the claim elements in the reference(s).

The Examiner has not provided a suggestion or motivation to combine the teachings of the references to provide the methods as claimed. Moreover, the applied references, alone or in combination, do not teach or suggest each and every element of Applicants' claims.

I. Lack of suggestion or motivation to combine the referenc s.

The Examiner has not provided a valid suggestion or motivation to combine and/or modify the disclosures of Hevey et al. and Huber et al. to provide the methods as recited in the claims. The Final Office Action does not provide any evidence of a suggestion or motivation in Hevey et al. to use the hapten-biotin conjugates of Huber et al., nor does the Office Action provide any evidence of a suggestion or motivation in Huber et al. to employ the conjugates in a heterogeneous immunoassay as described in Hevey et al..

A. No suggestion or motivation to combine elements of a homogeneous assay with elements of a heterogeneous assay.

The Examiner has asserted that Huber et al. at column 2, lines 50-54 provides a suggestion or motivation to combine the references in reciting the phrase "improved sensitivity" and "the rate of reaction is increased." However, this portion of the disclosure of Huber et al. is directed only to the use of specific hapten-biotin conjugates, and is not a general teaching about homogeneous assays. In the Advisory Action, it is further asserted that Huber et al. at col. 1, lines 1-34 "teaches embodiments that can be used in a homogeneous and heterogeneous assay methods" (page 2, lines 9-10 of Paper No. 17). However, this portion of the disclosure of Huber et al. is directed to a general background discussion of typical assay methods. At best, this portion of Huber et al. teaches that there are substantive differences between heterogeneous and

homogeneous assay methods, thus teaching away from combining techniques from these two general methods.

The Examiner has noted in the Advisory Action that the term "homogeneous assay" in the claims has not been examined as contributing to the substance of the claims, since the term appears in the preamble. Applicants respectfully point out that the differences between homogeneous and heterogeneous assays are, by definition, structural differences. According to the guidelines of MPEP § 2111.02, the term "homogeneous assay" in the preamble of the claims cannot be ignored, as this term describes the structure of the assays used in the claimed methods. Nevertheless, to ensure that the claims are examined in the context of homogeneous assays, claim 11 has been amended to recite that the claimed reaction mixture is a homogeneous assay reaction mixture. It is noted for the record that this amendment is a non-narrowing amendment, as the term "homogeneous assay" was already present as part of the substance of the claim.

Thus, no suggestion or motivation has been presented for combining the homogeneous system of Huber et al. with the heterogeneous sandwich assay disclosed in Hevey et al.. These assay systems are not simply interchangeable equivalents, and the combination proposed by the Examiner would render each approach unsatisfactory for its intended purpose.

B. No suggestion or motivation to provide identical or analogous 1st and 2nd haptens.

The Examiner has asserted that "identical haptens or its analogs have same or similar molecular weights or biological structure and contain the same or similar binding properties." This statement finds no support in the references and does not provide any connection to the disclosures of either of the references or to their combination. However, the Examiner has asserted that one skilled in the art would use identical haptens as a matter of an obvious design choice. Applicants respectfully point out that the Examiner's statements are insufficient to provide any suggestion or motivation to combine the cited references. As noted in MPEP § 2143.01, with reference to *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993):

> A statement that modifications of the prior art to meet the claimed invention would have been "'well within the ordinary skill of the art at the time the claimed invention was made'" because the references relied upon teach that all aspects of the claimed invention were individually known in the art is **not sufficient** to establish a *prima facie* case of obviousness without some **objective reason to combine** the teachings of the references. [Bold emphasis added]

The Advisory Action further asserts that Huber et al. teaches the use of identical haptens, with reference to claim 6 of the reference (page 2, lines 15-16 of Paper No. 17). Applicants respectfully point out that this aspect of Huber et al.

has already been addressed in the previous Amendment and Request for Reconsideration filed on July 30, 2003 (pages 15-16 of Paper No. 16). Thus, it has already been brought to the Examiner's attention that claim 6 of Huber et al. recites only that the hapten portion of an assay ingredient is identical to the analyte ("hapten to be determined"), not that it is identical to another assay ingredient. The Examiner has not refuted this fact and has not provided any other evidence that Huber et al. teaches or suggests a 2nd hapten or hapten-like molecule that is identical to a 1st hapten or hapten-like molecule, where both of these haptens are present as assay ingredients in an assay to determine an analyte.

Thus, the conclusory statements presented regarding obvious design choices of one skilled in the art are insufficient to establish a *prima facie* case of obviousness. The Examiner has not provided any evidence of a motivation or suggestion to combine the references, either from statements in the references themselves or from other documentary evidence on the record.

II. Lack of teaching or suggestion of each and every element of the claims

A. The references do not teach or suggest an assay component comprising a binding partner as claimed.

Even if Hevey et al. and Huber et al. were properly combined, the combination of the references would fail to provide each and every element of Applicants' claims. Specifically, neither Hevey et al. nor Huber et al. teach or suggest an assay component comprising a binding partner that binds both the 1st

and the 2nd hapten or hapten-like molecules, yet without interacting with the analyte. This assay component comprising a binding partner is one of three assay ingredients recited in claim 11 and in claim 19. The other two assay ingredients are (a) a haptenylated analyte specific component, which includes a 1st hapten or hapten-like molecule linked to an analyte specific component; and (b) a 2nd hapten or hapten-like molecule which is not linked to the analyte specific component, where the 2nd hapten or hapten-like molecule is identical to, or an analogue of, the 1st hapten or hapten-like molecule.

In the Final Office Action, the Examiner has correlated Applicants' assay component comprising a binding partner with the avidin disclosed in Hevey et al. (page 3, section 4 of Paper No. 15). Applicants respectfully disagree with this correlation, as the avidin of Hevey et al. does not bind to both a 1st hapten or hapten-like molecule and a 2nd hapten or hapten-like molecule according to the Examiner's own characterizations. If, as the Examiner asserts, the biotin of Hevey et al. is correlated with Applicants' 1st hapten and the enzyme of Hevey et al. is correlated with Applicants' 2nd hapten, then the binding partner (correlated with avidin) would bind only to the 1st hapten (avidin) and not the 2nd hapten (enzyme). In this scenario, the binding partner is already coupled to the 2nd hapten and would not bind to the 2nd hapten. Clearly, the embodiment constructed by the Examiner's correlations does not include each and every element of Applicants' claims.

In addition, the correlation of the enzyme of Hevey et al. with Applicants' 2nd hapten, as proposed by the Examiner, is not consistent with the specification. Although the Advisory Action asserts that page 4, lines 27-30 of the specification

"defines haptens to include enzymes," this assertion ignores the text surrounding the cited lines. The entire paragraph is as follows:

> The term hapten-like molecules is used to describe small molecules which are part of a non-immunological binding pair. Well known examples of such binding pairs are amongst others the prosthetic groups of enzymes and the enzyme, substrate derivatives and corresponding enzymes, biotin/avidin, or biotin/streptavidin. Preferably such hapten-like molecules are characterized by a molecular weight of less than 10 kD, more preferred less than 5 kD, more preferred less than 2 kD and most preferred less than 1 kD. Binding pairs comprising a hapten or hapten-like molecule and exhibiting rather high affinity are preferred. Preferably such affinity is at least 10^{-9} M/l, more preferred 10^{-10} M/l, most preferred 10^{-11} M/l or higher.
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> [specification, p. 4, line 27 – p. 5, line 5; emphasis added]

Thus, hapten-like molecules are defined as small molecules, such as substances having a molecular weight less than 10 kD. The hapten-like molecules are described as part of a binding pair. Although a given binding pair may include an enzyme, the actual hapten-like molecule is not an enzyme but rather may be, for example, a prosthetic group of an enzyme or a derivative of a substrate for an enzyme. This description is consistent with the definition of the term "haptens" at page 4, line 21 of the specification as "small molecules which themselves are not immunogenic." These definitions clearly excludes enzymes from the substances that can be haptens or hapten-like molecules.

Thus, the embodiment set forth as being disclosed by Hevey et al. does not teach or suggest an assay component comprising a binding partner as claimed, nor does it teach or suggest a 2nd hapten to which such an assay component could bind. Applicants note that the Examiner has asserted that Hevey et al. discloses several embodiments and variations of assays. However, without another characterization of Hevey et al. on the record, no correlation has been made between the disclosure of this reference and at least the assay component comprising a binding partner as recited in the claims.

The Huber et al. reference, alone or in combination with Hevey et al., also does not teach or suggest an assay component comprising a binding partner as recited in the claims. The Examiner has not set forth any characterizations of Huber et al. that would provide for this assay ingredient. Rather, Huber et al. has been applied to the present claims only as a possibility for modification of the assay method disclosed by Hevey et al. Accordingly, the applied references, alone or in combination, do not teach or suggest an assay component comprising a binding partner that binds both a 1st hapten or hapten-like molecule and a 2nd hapten or hapten-like molecule.

B. The references do not teach or suggest first and second haptens or hapten-like molecules as claimed.

The combination of Hevey et al. and Huber et al. fails to provide each and every element of Applicants' claims in that neither Hevey et al. nor Huber et al. teach or suggest a 1st hapten or hapten-like molecule linked to an analyte

specific component and a 2nd hapten or hapten-like molecule that is identical to, or an analogue of, the 1st hapten or hapten-like molecule. The Examiner has stated that Hevey et al. does not teach 1st and 2nd haptens or hapten-like molecules as recited in amended claims 11 and 19, but has asserted that Huber et al. discloses these elements (page 4, section 6 of Paper No. 15).

In the Final Office Action, the Examiner has asserted that Huber et al. discloses "the use of identical haptens or its analog". However, the only reference to the disclosure of Huber et al. is to column 2, lines 50-54, which appears to be a general statement about the benefits of hapten-biotin conjugates in homogenous immunoassays. As noted in section I.B. above, Applicants respectfully point out that the only disclosure in Huber et al. regarding two separate but identical haptens appears to be in claim 6 of the reference, which recites that "the hapten of said conjugate is identical to the hapten to be determined" (col. 8, lines 56-58). This claim limitation in Huber et al., however, is comparing the hapten portion of a hapten-biotin conjugate assay ingredient with the analyte ("hapten to be determined"), not with another assay ingredient. Huber et al. does not teach a 2nd hapten or hapten-like molecule that is identical to a 1st hapten or hapten-like molecule, where both of these haptens are present as assay ingredients in an assay to determine an analyte.

Neither Hevey et al., Huber et al., nor a combination of Hevey et al. and Huber et al. as characterized on the record teach or suggest each and every element of the pending claims. The references, alone or in combination, do not

teach or suggest an assay component comprising a binding partner that binds both the 1st and the 2nd hapten or hapten-like molecules, yet without interacting with the analyte. The references, alone or in combination, also do not teach or suggest a 1st hapten or hapten-like molecule linked to an analyte specific component and a 2nd hapten or hapten-like molecule that is identical to or an analogue of the 1st hapten or hapten-like molecule.

Accordingly, a *prima facie* case of obviousness over Hevey et al. in view of Huber et al. has not been presented. There is no evidence on the record of any suggestion or motivation to combine the disclosures of the references. Moreover, the combination of the references, even if proper, fails to teach or suggest each and every element of the claims. Claims 11-12, 14-15, 17-19, 21-23, 25 and 26 are not obvious under 35 U.S.C. § 103 over Hevey et al. in view of Huber et al., and Applicants respectfully request that this rejection be withdrawn.

CONCLUSIONS

In conclusion, all of the grounds raised for rejecting the application are believed to be overcome or rendered moot based on the remarks above. Thus, it is respectfully submitted that all of the presently presented claims are in form for allowance, and such action is requested in due course. Should the Examiner feel a discussion would expedite the prosecution of this application, the Examiner is kindly invited to contact the undersigned.

Respectfully submitted,

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